REMARKS

I. INTRODUCTION

Applicants thank the Examiner for participating in an interview between the Examiner and Applicants' representative on March 29, 2011 (the "Interview").

Claims 4-24, 28-36 and 44 have previously been cancelled, without prejudice. Claims 40-42 have previously been withdrawn. Applicants hereby reserve the right to pursue the cancelled and/or withdrawn claims in the above-identified application and/or one or more continuation and/or divisional applications claiming priority to the above-identified application. Claims 1-3, 25-27, 37-39, 43 and 45-64 of the above-identified application are under consideration.

II. INTERVIEW SUMMARY

During the Interview, Applicants' representative and the Examiner discussed claims independent claim 1, 25 and 37, and claim 49 which depends from independent claim 1. In particular, the rejection under 35 U.S.C. § 103 were discussed with respect to the above-identified claims as allegedly being unpatentable over Delenstarr et al., "*Estimation of the confidence limits of oligonucleotide array-based measurements of differential expression*," Proceedings of SPIE, vol. 4266, pp. 120-131 (2001) (the "Delenstarr Publication"), in view of *Z-Score*, The Concise Corsini Encyclopedia of Psychology and Behavioral Science (2004) (the "Z-Score Reference") and International Patent Publication WO 99/49403 published September 30, 1999 by Lincoln et al. (the "Lincoln Publication").

During the Interview, Applicants asserted that the Delenstarr Publication does not teach or suggest that, *inter alia*, **the determination of a plurality of subintervals is performed by *repeatedly* dividing an interval until a criteria is met**, as explicitly recited in independent claims 1, 25 and 37 of the above-identified application. The Examiner contended in the discussion that dividing an interval into multiple subintervals, e.g., to yield the histogram illustrated in the Delenstarr Publication, is purportedly equivalent to repeatedly dividing an interval. Applicants respectfully disagreed with this contention by the Examiner during the Interview and discussed potentially submitting a response with either additional arguments and/or claim amendments and/or additions.

Further, Applicants' representatives brought to the Examiner's attention that the Delenstarr Publication, contrary to the Examiner's assertion in the Final Office Action, also fails to teach or suggest a dyadic grid at all, *much less* that the subintervals are determined based on a dyadic grid division procedure, as explicitly recited in claims 49 and 57. The Examiner invited Applicants to include such arguments in a response for further consideration.

Further, during the Interview, the Examiner confirmed that upon Applicants submitting arguments in a response to the final Office Action, and the Examiner being persuaded that at least one of the claims of the present application overcome the § 103 rejection of such respective claim(s), the Examiner would withdraw the finality of the present Office Action, and reopen prosecution of the present application accordingly.

III. REJECTION UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

Claims 1-3, 25-27, 37-39, 43 and 45-64 stand finally rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Delenstarr et al., "*Estimation of the confidence limits of oligonucleotide array-based measurements of differential expression*," Proceedings of SPIE, vol. 4266, pp. 120-131 (2001) (the "Delenstarr Publication"), in view of *Z-Score*, The Concise Corsini Encyclopedia of Psychology and Behavioral Science (2004) (the "Z-Score Reference") and International Patent Publication WO 99/49403 published September 30, 1999 by Lincoln et al. (the "Lincoln Publication"). (*Id.*, p. 4).

Applicants respectfully assert that the Delenstarr Publication, taken alone or in alleged combination with the Z-Score Reference and the Lincoln Publication fails to teach or suggest the subject matter recited in independent claims 1, 25 and 37 and the claims which depend therefrom, respectfully, for at least the reasons set forth herein below.

"To reject claims in an application under Section 103, an examiner must show an unrebutted *prima facie* case of obviousness." *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1455 (Fed. Cir. 1998). The Supreme Court in *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966), stated:

> Under Section 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined.

Indeed, to sustain a rejection under 35 U.S.C. § 103(a), there must be some teaching, other than the instant application, to alter the prior art to arrive at the claimed invention. "The problem confronted by the inventor must be considered in determining whether it would have been obvious to combine the references in order to solve the problem." *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 679 (Fed. Cir. 1998).

The objective standard for determining obviousness under 35 U.S.C. § 103, as set forth in *Graham v. John Deere, Co.*, 383 U.S. 1 (1966), requires a factual determination to ascertain: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; and (3) the differences between the claimed subject matter and the prior art. Based on these factual inquiries, it must then be determined, as a matter of law, whether or not the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the alleged invention was made. *Graham*, 383 U.S. at 17. Courts have held that there must be some suggestion, motivation or teaching of the desirability of making the combination claimed by the applicant (the "TSM test"). *See In re Beattie*, 974 F.2d 1309, 1311-12 (Fed. Cir. 1992). This suggestion or motivation may be derived from the prior art itself, including references or disclosures that are known to be of special interest or importance in the field, or from the nature of the problem to be solved. *Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Cir. 1996).

Although the Supreme Court criticized the Federal Circuit's application of the TSM test, *see KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, (2007) the Court also indicated that the TSM test is not inconsistent with the *Graham* analysis

recited in the *Graham v. John Deere* decision. *Id.*; *see In re Translogic Technology, Inc.*, No. 2006-1192, 2007 U.S. App. LEXIS 23969, *21 (October 12, 2007). Further, the Court underscored that "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR*, 127 S. Ct. at 1741. Under the precedent established in *KSR*, however, the presence or absence of a teaching, suggestion, or motivation to make the claimed invention is merely one factor that may be weighed during the obviousness determination. *Id.* Accordingly, the TSM test should be applied from the perspective of a person of ordinary skill in the art and not the patentee, but that person is creative and not an automaton, constrained by a rigid framework. *Id.* at 1742. However, "the reference[s] must be viewed without the benefit of hindsight afforded to the disclosure." *In re Paulsen*, 30 F.3d 1475, 1482 (Fed. Cir. 1994).

The prior art cited in an obviousness determination should create a reasonable expectation, but not an absolute prediction, of success in producing the claimed invention. *In re O'Farrell*, 853 F.2d. 894, 903-04 (Fed. Cir. 1988). Both the suggestion and the expectation of success must be in the prior art, not in applicant's disclosure. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1207 (Fed. Cir. 1991) (citing *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988)). Further, the implicit and inherent teachings of a prior art reference may be considered under a Section 103 analysis. *See In re Napier*, 55 F.3d 610, 613 (Fed. Cir. 1995).

Secondary considerations such as commercial success, long-felt but unsolved needs, failure of others, and unexpected results, if present, can also be

considered. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538-39 (Fed. Cir. 1983). Although these factors can be considered, they do not control the obviousness conclusion. *Newell Cos. v. Kenney Mfg. Co.*, 864 F.2d 757, 768 (Fed. Cir. 1988).

Absence of a property which a claimed invention would have been expected to posses based on the teachings of the prior art is evidence of nonobviousness. *Ex parte Mead Johnson & Co.* 227 USPQ 78 (Bd. Pat. App. & Inter. 1985). Evidence of unobvious or unexpected advantageous properties can rebut *prima facie* obviousness. *In re Chupp*, 816 F.2d 643, 646 (Fed. Cir. 1987).

To establish obviousness, the prior art references must be evaluated as a whole for what they fairly teach and neither the references' general nor specific teachings may be ignored. *Application of Lundsford*, 357 F.2d. 385, 389-90 (CCPA 1966). A reference must be considered for all that it teaches, not just what purportedly points toward the invention but also that which teaches away from the invention. *Ashland Oil, Inc. v. Delta Resins & Refractories*, 776 F.2d. 281, 296 (Fed. Cir. 1985).

Independent claims 1, 25 and 37 recite, *inter alia*, process, non-transitory storage medium and system, respectively, at least one interval associated with a dataset is determined, **the determination of a plurality of subintervals of the at least one interval is performed by *repeatedly dividing* the at least one interval until at least one predetermined criteria is met**, and **the determination of statistically-outlying data points present in the at least one dataset is performed based on information related to the subintervals, where each particular data point of the statistically-outlying data points is (i) associated with a particular interval of the**

subintervals, and (ii) determined as a function of a length of the particular subinterval of the subintervals associated with the particular data point.

The Delenstarr Publication relates to, e.g., "[e]stimation of the confidence limits of oligonucleotide microarray-based measurements of differential expression." (*Delenstarr Publication*, Title). In particular, this publication describes a method that "used a combination of fluor-exchanged two-color labeling and improved normalization methods to minimize systematic errors from labeling bias, imperfect features, and mismatched sample concentrations." (*Id.*, Abstract). According to the Delenstarr Publication, "[o]n-microarray specificity control probes and experimentally proven probe design algorithms were used to correct for cross-hybridization." (*Id.*) "Random errors were reduced via automated non-uniform feature flagging and an advanced scanner design." (*Id.*) "[F]eature significance [was scored] using established statistical tests." (*Id.*) "[T]he intrinsic random measurement error [was then estimated] as a function of average probe signal via sample self-comparison experiments (human K-562 cell mRNA)." (*Id.*)

The Z-Score Reference provides an encyclopedia definition of *Z-Score*. For example, the Z-Score Reference describes that "[t]he z-score, also known as the standard score, is the result of a transformation of raw data, and this conversion can be summed up as follows: Something minus its mean divided by its standard deviation." (*Z-Score Reference*, first paragraph).

The Lincoln Publication "relates generally to bioinformatics, and particularly to a system and method for analyzing bimolecular sequences." (*Lincoln Publication*, p.1, lns. 6-7).

Applicants respectfully assert that the Delenstarr Publication does not at all teach, suggest or disclose any process, storage medium or system using which the determination of a plurality of subintervals is performed by ***repeatedly dividing* an interval** until a criteria is met, *much less* that the determination of statistically-outlying data points present in the dataset is performed based on information related to the subintervals, *much less still* where each of the statistically-outlying data points is associated with a particular subinterval, and determined as a function of the length of such subinterval, as explicitly recited in independent claims 1, 25 and 37 of the above-identified application.

In the Final Office Action, the Examiner alleges that "[t]he abscissa axes of Figure 1b of Delenstarr et al. illustrate the intervals associated with each of the red and green channels [and that t]his interval is broken down into subintervals in the form of widths of histogram bars." (Final Office Action, p. 4). The Examiner then contends that "[i]n other words, the intervals of Figure 1b of Delenstarr et al. are divided into subintervals until the criterion of the entire histogram being displayed with the bars of the given width is met." (*Id.*). The Examiner further purports that "[t]he data within the histograms are considered to be outlying data if the histogram bar is more than two standard deviations away on either side on (sic) the mean" and relies on "the last full paragraph of page 121" of this publication in alleged support of this contention. (*Id.*)

The Examiner then believes that "in determining whether a histogram bar corresponds to an outlier, the data point is associated with the subinterval that encompasses it, which, in turn, is determined as a function of length from the mean (in this instance, length is the number of standard deviations from the mean)." (*Id.*, pp. 4-5)

However, Applicants respectfully assert that the Examiner's interpretation of the Delenstarr Publication is flawed, and that the Delenstarr Publication certainly does not even teach or suggest the subject matter based on such flawed interpretation. As described in the Delenstarr Publication, "[t]he example in Figure 1b [thereof] shows pixel histograms from both the green and red channels of a feature." (Delenstarr Publication, p. 121, section 3.1.1). "This example used the mean ± 2 standard deviations (SD) of the population as the range for inlier pixels." (*Id.*) "Those pixels outside of this range are deemed outliers and are removed from further calculations." (*Id.*) "A new mean and standard deviation are then calculated for each feature, using only the inlier pixels." (*Id.*) "This process is performed for each feature and each feature's local background region, in both the green and red channels." (*Id.*)

First, Applicants respectfully assert that each of the pixel histograms from both the green channels and the red channels of a feature (that is illustrated in Figure 1b of the Delenstarr Publication) is certainly not (and cannot be) equivalent to the interval as recited in independent claims 1, 25 and 37 of the above-identified application, as such purported correspondence would not make sense. The Examiner even acknowledges that the histograms of Figure 1b of the Delenstarr Publication

represent two separate histograms of signals (one for the green channel and the second for the red channel). (See Final Office Action, p. 8).

Second, even if, assuming *arguendo*, that each of these histograms are interpreted as being equivalent to the recited interval (with which interpretation Applicants disagree), the widths of histogram bars of the Delenstarr Publication) are certainly not equivalent to the sub-intervals as recited in independent claims 1, 25 and 37. Rather, as described in the Delenstarr Publication, Figure 1b of the Delenstarr Publication indicates two separate histograms of signals, i.e., one for the Green channel, and one for the Red channel) representing pixels. (See, e.g., Delenstarr Publication, Figure 1b).

Third, contrary to the Examiner's contention and as discussed during the Interview, the histograms and the histogram bars of the Delenstarr Publication are **not *repeatedly* divided** until a criteria is met in a determination of a plurality of subintervals, which is required in independent claims 1, 25 and 37. Indeed, the Delenstarr Publication does not teach or suggest ***repeatedly* dividing an interval** *at all*. Rather, as described in the Delenstarr Publication, "pixels outside of [the mean ± 2 standard deviations] range are deemed outliers and are removed [and a] new mean and standard deviation are then calculated for each feature." (*Id.*, p. 121, section 3.1.1). Thus, no "subdivision" occurs in the Delenstarr Publication whatsoever. Applicants respectfully assert that one having ordinary skill in the art would have understood that removing the histogram bars representing outliers (> 2 standard deviations from the mean) before performing further calculations is certainly not any **division of an interval**, *much less* a

repeated* division**, as explicitly recited in independent claims 1, 25 and 37 of the above-identified application. Even if the bars of the histogram are, *arguendo*, equated to being divided into intervals, such division is not performed ***repeatedly, as explicitly recited in independent claims 1, 25 and 37.

Indeed, **repeatedly is defined as, e.g., "more than once; again and again"**. (See, *e.g.*, Free Online Dictionary, available at http://www.thefreedictionary.com/p/repeatedly, last accessed March 30, 2011, and the Merriam-Webster dictionary, available at http://www.merriam-webster.com/dictionary/repeatedly, last accessed March 30, 2011). Applicants respectfully assert that, even under the Examiner's strained interpretation of the Delenstarr Publication, dividing an interval into multiple subintervals is not equivalent to repeatedly dividing an interval. Rather, under the broadest reasonable interpretation, the abscissa axes of Figure 1b of the Delenstarr Publication merely illustrate an interval **divided *once*** into multiple subintervals in the form of widths of histogram bars. The histogram bars are not divided. Indeed, there is no interval that is divided again, i.e., more than once. Thus, there is certainly **no *repeated* division of an interval** taught or suggested in the Delenstarr Publication whatsoever.

Fourth, Applicants respectfully assert that the Examiner's contention in the Office Action that the "length [***of a particular subinterval***] is the number of standard deviations from the mean" is *counter* to the Examiner's further contention in the same paragraph of the Office Action that the widths of the histogram bars are allegedly equivalent to the recited subintervals and that "histograms are considered to be outlying

data if the histogram bar is more than two standard deviations away on either side of the mean." (Office Action, p. 6). Indeed, **it is not possible** for a histogram bar to be more than two standard deviations away from the mean if the width of the histogram bar is equivalent to a subinterval having a length equal to the number of standard deviations from the mean, as purported by the Examiner on pages 5 and 6 of the Office Action.

Thus, Applicants respectfully assert that the Delenstarr Publication certainly does not teach or suggest any process, storage medium or system using which the determination of a plurality of subintervals is performed by ***repeatedly dividing an interval*** until a criteria is met, *much less* that the determination of statistically-outlying data points present in the dataset is performed based on information related to the subintervals, *much less still* where each of the statistically-outlying data points is associated with a particular subinterval, and determined as a function of the length of such subinterval, as explicitly recited in independent claims 1, 25 and 37 of the above-identified application.

It is further respectfully asserted that the Z-Score Reference and the Lincoln Publication fail to cure at least the deficiencies of the Delenstarr Publication that are described herein above, and the Examiner does not assert that these publications do.

Therefore, for at least the reasons provided herein above, the rejection of independent claims 1, 25 and 37, claims 2, 3, 43 and 47-54 which depend from independent claim 1, claims 26, 27, 45 and 55-62 which depend from amended independent claim 25, and claims 38, 39, 46, 63 and 64 which depend from

independent claim 37, under 35 U.S.C. § 103(a) as allegedly being unpatentable over the Delenstarr Publication, in view of the Z-Score Reference and the Lincoln Publication, should be withdrawn.

With further respect to claims 49, 57, 63 and 64, which depend from independent claims 1, 25 and 37, as applicable, each of these claims recites that, *inter alia*, *the subintervals are determined based on* ***a dyadic grid division procedure***. Applicants respectfully assert that, contrary to the assertion by the Examiner on page 6 of the Final Office Action, **the Delenstarr Publication fails to teach or suggest a dyadic grid** at all, *much less* **that the subintervals are determined based on a dyadic grid division procedure**, as explicitly recited in claims 49, 57, 63 and 64. "In mathematics, a **dyadic fraction** or **dyadic rational** is a rational number whose denominator is **a power of two**, i.e., a number of the form a/2b where a is an integer and b is a natural number; for example, 1/2 or 3/8, but not 1/3." (See, e.g., Wikipedia Online Encyclopedia, dyadic rationale, available at http://en.wikipedia.org/wiki/Dyadic_fraction, last accessed March 30, 2011).

In addition, paragraphs [0025] – [0027] of the Specification and Figure 1 of the present Application describe and illustrate how, e.g., **subintervals can be determined based on a dyadic grid division procedure** in accordance with an exemplary embodiment of such a procedure, as recited in claims 49, 57, 63 and 64. Indeed, there is simply no teaching or suggestion whatsoever in the Delenstarr Publication of a dyadic rationale, dyadic function, or dyadic grid. Thus, it certainly follows that the Delenstarr Publication fails to teach or suggest that **subintervals are**

determined based on a dyadic grid division procedure, as explicitly recited in claims 49, 57, 63 and 64 of the above-identified application. Further, Applicants respectfully assert that the Z-Score Reference and the Lincoln Publication fail to cure at least these additional deficiencies of the Delenstarr Publication described herein above (e.g., with respect to 49, 57, 63 and 64), and the Examiner does not assert that these publications do.

Moreover, **with further respect to claims 51, 59, 63 and 64**, which depend from independent claims 1, 25 and 37, as applicable, each of these claims recites that, *inter alia*, **each particular subinterval of the subintervals comprises a respective region having a height, where the height is determined as a function of the length of the subinterval, and where each of the statistically-outlying data points is located outside of the respective region of the particular subinterval with which the statistically-outlying data point is associated**.

Applicants respectfully assert that the Delenstarr Publication, even if taken in alleged combination with the Z-Score Reference and the Lincoln Publication, fails to teach or suggest at least that **each particular subinterval of the subintervals comprises a respective region having a height, where the height is determined as a function of *the* length of the subinterval, and where each of the statistically-outlying data points is located outside of the respective region of the particular subinterval with which the statistically-outlying data point is associated**.

In the Final Office Action, the Examiner alleges that "each of the bars in the histogram has a height that is a function of length/position on the abscissa." (Office

Action, p. 7). However, even based on the Examiner's interpretation of Delenstarr, length/position on the abscissa is not equivalent to ***the* length of the subinterval**, as explicitly recited in claims 51, 59, 63 and 64.

Indeed, during the Interview with respect to the recitation in independent claims 1, 25 and 37 of ***a* length** of the particular subinterval, the Examiner contended that such length can be virtually any length due to usage of the pronoun "a" there before. Further, the Examiner indicated that if "a" had been amended to "the" in the amendment filed in response to the previous, non-final Office Action, that such length would have been properly interpreted by the Examiner as being ***the* length of the particular subinterval**. Accordingly, Applicants respectfully assert that, based on the Examiner's own reasoning, the explicit recitation in claims 51 and 59 ***the* length of the subinterval** and in claims 63 and 64 of ***the* length of the particular subinterval**, the Examiner's contention in the latest Office Action that "each of the bars in the histogram has a height that is a function of length/position on the abscissa" is in no way equivalent to ***the* length of the subinterval**, as explicitly recited in claims 51, 59, 63 and 64.

Thus, it certainly follows that the Delenstarr Publication, even if taken in alleged combination with the Z-Score Reference and the Lincoln Publication, fails to teach or suggest at least that **each particular subinterval of the subintervals comprises a respective region having a height, where the height is determined as a function of *the* length of the subinterval, and where each of the statistically-outlying data points is located outside of the respective region of the particular**

subinterval with which the statistically-outlying data point is associated, as explicitly recited in claims 51, 59, 63 and 64 of the above-identified application.

IV. CONCLUSION

In light of the foregoing, Applicants respectfully submit that all claims under consideration 1-3, 25-27, 37-39, 43 and 45-64 and are in condition for allowance. Prompt consideration, reconsideration and allowance of all of the claims of the above-identified application are therefore earnestly solicited. If any issues remain outstanding, the Examiner is invited to contact the undersigned via the telephone number provided below.

Respectfully submitted,

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